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EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/917,384

Applicant(s)

ADNEY ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 January 2005.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11, 14-25, 28-35, 44, 45 and 69-78 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 75-77 is/are allowed.
- 6) ☒ Claim(s) 1-5, 14-25, 28-35, 44, 45 and 69-74 is/are rejected.
- 7) ☒ Claim(s) 6-11 and 78 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>12-3-01</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-11, 14-25, 28-35, 44-45, 69-78 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 5-24-04, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Examiner notes that the Office has granted applicant's petition to withdraw the previously held abandonment. Examiner also acknowledges the filing of the declaration by Dr. Himmel in support of the arguments traversing the rejections under 35 U.S.C. 112, 1<sup>st</sup> paragraph.

### ***Sequence Compliance***

It is noted that applicant has filed a sequence listing on 1-24-05. However, it is not clear to the Examiner whether said sequence listing is identical to that filed previously on 11-27-02 or whether said sequence listing is an amended version. Furthermore, applicant has failed to provide the computer readable copy of the sequence listing and has thereby failed to comply with sequence rules and requirements. Therefore, Examiner has not considered the sequence listing filed on 1-24-05 and states for the record that all searches and rejections are based on the previous version of the sequence listing. See particularly 37 CFR 1.821(d).

### ***Claim Objections***

Claim 11 is objected to because of the following informalities: Claim 11 is drawn to SEQ ID NO:2. However, claim 11 improperly recites SEQ ID NO:2 as an amino acid sequence.

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It can be seen from the sequence listing that SEQ ID NO:2 is a polynucleotide and not a polypeptide. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 14-25, 28-35, 44-45, 69-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Gux 1 polypeptide comprising a catalytic domain with SEQ ID NO:5, further comprising a CBD-III domain with SEQ ID NO:4 and a CBD-II domain with SEQ ID NO:7, or a peptide having SEQ ID NO:1 encoded by a nucleic acid sequence with SEQ ID NO:1, does not reasonably provide enablement for any or all such Gux I peptide comprising a catalytic domain of any 637 to about 643 amino acids in length or any CBDIII domain that is about 150-156 amino acids in length or any CBDII domain that is 95-105 amino acids in length or an amino acid sequence that is 90% identical to SEQ ID NO:1 or encoded by a polynucleotide that is 90% identical to SEQ ID NO:2, or a Gux1 peptide comprising a catalytic domain that is 70%, 80%, 90% to SEQ ID NO:5 and/or a CBD domain that is 90% identical to SEQ ID NO:7 or a peptide comprising amino acid sequence that is 70% or at least 90% identical to SEQ ID NO:4, 5, 6, 7 or 1 and fusion polypeptides of the above polypeptides comprising a heterologous polypeptide such a peptide tag, or a substrate targeting moiety or a composition comprising such polypeptides along with a carrier. The specification

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does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5, 14-25, 28-35, 44-45, 69-74 are so broad as to encompass any glycosylhydrolase polypeptide comprising a catalytic domain of any 637 to about 643 amino acids in length or any CBDIII domain that is about 150-156 amino acids in length or any CBDII domain that is 95-105 amino acids in length or an amino acid sequence that is 90% identical to SEQ ID NO:1 or encoded by a polynucleotide that is 90% identical to SEQ ID NO:2, or a Gux1 peptide comprising a catalytic domain that is 70%, 80%, 90% to SEQ ID NO:5 and/or a CBD domain that is 90% identical to SEQ ID NO:7 or a peptide comprising amino acid sequence that is 70% or at least 90% identical to SEQ ID NO:4, 5, 6, 7 or 1 and fusion polypeptides of the above polypeptides comprising a heterologous polypeptide such a peptide tag, or a substrate targeting moiety or a composition comprising such polypeptides along with a carrier.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of Gux1 polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence

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and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one such Gux1 polypeptide with SEQ ID NO: 1 encoded by SEQ ID NO:2. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides some even with an undefined function/activity. The specification is limited to teaching use of SEQ ID NO: 1 or a polypeptide comprising polypeptides with SEQ ID NO:4, 5 and 7 as a Gux1 polypeptide but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art

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would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any glycosylhydrolase polypeptide as described in the above paragraphs because the specification does not establish: (A) regions of the protein structure which may be modified without effecting either the catalytic activity or the cellulose binding activity of the CBD domains; (B) the general tolerance of glycosylhydrolases such as cellulase or endoglucanases and the CBDs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any glycosylhydrolase or any CBD polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including glycosylhydrolase catalytic domains, and cellulose binding domains with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

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In response to the previous Office action, applicants have traversed the above rejection basically arguing that claims are enabled. Applicants have also filed a Rule 1.132 Declaration by Dr. Himmel which also argues that claims are enabled. Applicants argue that Office is in error to assert that the disclosure teaches nothing germane to the scope of the claims other than SEQ ID NOS 1, 2, 4, 5 and 7. Applicants argue that the disclosure teaches the use of family GH48, CBDII and CBDIID domains in combination and that the Declaration provides evidence of 16 GH48 family enzymes, 125 instances of CBDII domains and 66 instances of CBDIID domains listed in CAZy site index with cross-reference to other databases. Applicants assert that these elements identified in CAZy can be combined in approximately 132,000 different combinations of three elements and the specification provides guidance to combine these families as recited in the broader claims. Applicants do concede that although the exact sequences are not specifically disclosed in the present specification except by reference to family, it is sufficient in this art to provide guidance directing practitioners to the combination of well known domain families and that a patent need not teach and preferably omits what is well known in the art. Examiner respectfully disagrees with the above line of argument and concludes that applicants have misunderstood the whole rejection. Examiner asserts that he is not questioning the enablement of combining the three different sequences to form a fusion protein as claimed. Applicants should also note that their claims are not simply limited to the those sequences that are found on the CAZy databases even though the number is 132,000. The claims in question are much broader and the total number of sequences encompassed may be much higher than 132,000 for which applicants have no support in the specification. As stated in the above rejection specification lacks support for enabling above claims because it does not provide guidance as to



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how those skilled in the art can make variants and mutants that have 70%, 80% or 90% sequence identity to SEQ ID NO:1, 2, 4, 5 or 7. Applicants' arguments are not persuasive because while the specification may direct practitioners of the art to databases that provide a large number of specific sequences of the three domains, specific guidance to produce variants of the three domains as claimed in the instant claims are not provided in the specification. While general methods to produce variants of known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants as claimed by applicants requires that one of ordinary skill in the art know or be provided with specific guidance regarding the amino acid residues in the sequence that can be modified without affecting its activity (in the instant case the catalytic activity of the glycosyl hydrolase of GH48 family) and guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities of the amino acid sequences. This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting either the catalytic activity or the cellulose binding activity of the CBD domains; (B) the general tolerance of glycosylhydrolases such as cellulase or endoglucanases and the CBDs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any glycosylhydrolase or any CBD polypeptide

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amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Claims 1-5, 22-25, 69-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5, 22-25, 69-74 are directed to composition comprising a Gux1 peptide wherein said Gux1 peptide comprises a catalytic domain GH48 of 637 to 643 amino acids in length, a carbohydrate binding domain CBD type III of 15-156 amino acids in length and a CBD type II of 95-105 amino acids in length and fusion polypeptides of the same fused to heterologous polypeptides all of which encompass variants, mutants and recombinants. Claims 1-5, 22-25, 69-74 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue (i.e., variants and mutants) that have not been disclosed in the specification. No description has been provided of even a representative number of polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 or characterization of SEQID NO:4-7 as catalytic domains and CBD domains, has been provided by applicants which would indicate that they had possession of the claimed genus of all the polypeptides. The specification does not contain any disclosure of the structure of the polypeptide sequences, including fragments and variants within

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the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

In response to the previous Office action, applicants have traversed the above rejection arguing that patents need not teach what is already well known in the art, that those skilled in the art would have the knowledge to modify the amino acid sequence with SEQ ID NO:1 and that such techniques for modification are well known. Applicants also recite from the *Amgen Inc. v. Hoechst Marion Rousel Inc.* case and the decision handed in that particular case. Applicants also refer to the more recent *Enzo Biochem* case. While the Examiner has no objections to those decisions handed down by the courts, the same decisions cannot be extended to the instant claims and be argued that the above rejection needs to be withdrawn. Examiner has in fact rewritten the above rejection so that it makes it clear to the applicants as to why the above rejection has been applied. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by

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disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of claims 1-5, 22-25, 69-74 includes species which are widely variant in structure ( including all those that disclosed in the different the electronic databases recited in the Declaration by Himmel). The genus of claims 1-5, 22-25, 69-74 is structurally diverse as it encompasses polypeptides with Gux1, glycosylhydrolase activity/cellulose binding activity from all or any source. As such, neither the description of the function of the Gux1 polypeptide nor the disclosure solely of functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

The Declaration filed by Dr. Himmel is also not persuasive to overcome the above rejection. This is because while the Declaration declares that the three domains are well known and that those practicing the art can arrive at the sequences by going to the CAZy database web

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site it does not address providing the description of the structure of variants and mutants encompassed in the above claims. Hence the above rejection is maintained.

Claims 28-35, 44-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 28-35, 44-45 are directed to composition comprising an amino acid with SEQ ID NO:4, 5, 6, or 7 or polypeptides comprising amino acid sequences that are 70% identical to SEQ ID NO: 4, 5, 6, or 7 and fusion polypeptides comprising the above amino acid sequences.

Claims 28-35, 44-45 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides whose function has not been described. No description has been provided of the all the polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 and 5 as a Gux1 polypeptide with a glycosylhydrolase activity or partial characterization of SEQID NO:4 and 7 as having cellulose binding activity, has been provided by applicants which would indicate that they had possession of the claimed genus of all the polypeptides. The specification does not contain any disclosure of the function of all the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of function. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the

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art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

In response to the previous Office action, applicants have traversed the above rejection arguing that patents need not teach what is already well known in the art, that those skilled in the art would have the knowledge to modify the amino acid sequence with SEQ ID NO:1 and that such techniques for modification are well known. Applicants also recite from the *Amgen Inc. v. Hoechst Marion Rousel Inc.* case and the decision handed in that particular case. Applicants also refer to the more recent *Enzo Biochem* case. While the Examiner has no objections to those decisions handed down by the courts, the same decisions cannot be extended to the instant claims and be argued that the above rejection needs to be withdrawn. Examiner has in fact rewritten the above rejection so that it makes it clear to the applicants as to why the above rejection has been applied. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means

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that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genera of claims 28-35, 44-45 includes species which are widely variant in function. The genus of claims 28-35, 44-45 is functionally diverse as it encompasses polypeptides comprising amino acid sequences that are 70% or 90% identical to SEQ ID NO:4-7 or 1 without any attached function to such polypeptides. As such, neither the description of the structure of one single Gux1 polypeptide (SEQ ID NO:1 or 5) or the CBD polypeptides (SEQ ID NO:4, 7), nor the disclosure solely of structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus. The Declaration filed by Dr. Himmel is also not persuasive to overcome the above rejection. This is because while the Declaration declares that the three domains are well known and that those practicing the art can arrive at the sequences by going to the CAZy database web site it does not address providing the description of the function of variants and mutants encompassed in the above claims. Hence the above rejection is maintained.

***Conclusion***

Claims 75-77 are allowable.

Claims 6-10, 78 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Examiner has withdrawn the previous rejection of claims 14-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, in view of the claim amendments.

Examiner has withdrawn the previous rejection of claims 1-3, 6-10, 14-25, 28-35, 44-45, 69-74 as obvious under 35 U.S.C. 103(a) over Zverlov et al. and Tomme et al. in view of the arguments presented by the applicants.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

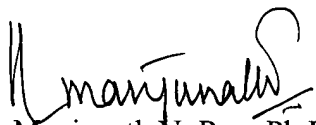
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,



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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

  
Manjunath N. Rao, Ph.D.  
Primary Examiner  
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June 29, 2005